General

Guideline Title

Ciclosporin for treating dry eye disease that has not improved despite treatment with artificial tears.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Ciclosporin for treating dry eye disease that has not improved despite treatment with artificial tears. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Dec 16. 45 p. (Technology appraisal guidance; no. 369).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Ciclosporin is recommended as an option, within its marketing authorisation, for treating severe keratitis in adult patients with dry eye disease (DED) that has not improved despite treatment with tear substitutes.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Dry eye disease (DED) (also called dry eye syndrome and sometimes 'keratitis')

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Family Practice

Ophthalmology

Intended Users

Physicians

Guideline Objective(s)

To assess the clinical effectiveness and cost-effectiveness of ciclosporin for treating dry eye disease (DED) that has not improved despite treatment with artificial tears

Target Population

People with severe dry eye disease (DED) whose disease has not adequately responded to tear substitutes

Interventions and Practices Considered

Ciclosporin

Major Outcomes Considered

- Clinical effectiveness
  - Efficacy outcomes
    - Corneal fluorescein staining (CFS) score assessed with a variety of scales
    - Ocular surface disease index (OSDI) score
    - Visual analogue scale (VAS) score
    - Schirmer-I test score (without anaesthesia)
    - Tear-film break-up time (TBUT)
    - Complete corneal clearing
    - Artificial tear use
    - Investigator global evaluation of efficacy
  - Safety outcomes
    - Grade 3/4 adverse events (AE) only
    - Overall incidence of AE
    - Withdrawal due to AE
    - Serious adverse events (SAE)
    - Individual AE: blepharitis, eye irritation, instillation site pain, eye pain, conjunctival hyperaemia and nasopharyngitis
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by Liverpool Reviews & Implementation Group (LRiG) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Critique of the Methods of Review(s)

Searches

The search strategies used to identify papers for the company's systematic review are described in the company's submission (CS). These searches were conducted in Medline, Medline In-process, EMBASE (all OVID SP) and CENTRAL (via the Cochrane library). They were carried out on 21 July 2014 and the databases were searched from inception to that date. PubMed was also searched, but limited to e-publications ahead of print. No grey literature Web sites were searched but the company did search for relevant conference proceedings. Overall, the ERG considers the search strategies to be sufficiently comprehensive and the search terms to be relevant for this drug and condition. However, limiting the searches of the Cochrane library databases to CENTRAL was unusual and risked missing relevant studies via other sources, such as any studies included in systematic reviews identified via the Cochrane Database of Systematic Reviews.

To ascertain whether the company had missed any relevant studies the ERG conducted its own searches (summarised in Appendix 1, section 10.1 of the ERG report). The ERG's search, conducted on 22 December 2014, identified two recently published systematic reviews of ciclosporin (CsA) for the treatment dry eyes disease (DED) of any severity. Included in these systematic reviews were additional randomised controlled trials (RCTs) not included by the company.

Eligibility Criteria

The eligibility criteria for the systematic review are reported in the CS and reproduced in the table below. The population is compatible with that outlined in the company's decision problem. However, the ERG notes that the intervention is Ikervis, which is more specific than 'ciclosporin', the intervention specified in both the NICE scope and the company's decision problem. Additional comparators and outcomes were also included. For the systematic review, these include other formulations of CsA which the ERG considers are the most relevant comparators to Ikervis. Other comparators, including punctal plugs, permanent punctal occlusion and autologous serum, are considered by the ERG to be of less relevance to the NICE scope or company's decision problem. This is because these are likely to be treatment options after failure of CsA rather than as alternatives to CsA. Indeed, in the company's economic model, punctal plugs are a treatment option for patients following treatment with Ikervis. In terms of outcomes, while the ERG considers the additional outcomes to be relevant to the NICE scope and company's decision problem, including or excluding studies based on outcomes is not recommended as it may introduce reporting bias.

Eligibility Criteria Used for the Company's Systematic Review

Patients	Adult patients (≥18 yr) with severe keratitis with dry eye disease (DED) which has not improved despite treatment with tear substitutes. Severe DED was defined as follows: • Dry Eye Workshop (DEWS) 3 or 4 or two of the following criteria being met: 1. Schirmer's test score (with or without anaesthesia) ≤5 mm/5min 2. Tear-film break-up time (TBUT) score ≤5 seconds 3. Ocular Surface Disease Index (OSDI) ≥23 (0 to-100 scale)
Intervention	Ciclosporin-A (Ikervis)
Comparators	• Ciclosporin-A (CsA) • Punctal plugs • Permanent punctal occlusion

	• Autologous serum • Artificial tears • Cholinergic agonists • Acetylcysteine drops • Topical corticosteroids
Outcomes	Efficacy Outcomes • Corneal fluorescein staining (CFS) score assessed with independent scales • OSDI score • Visual analogue scale (VAS) score • Schirmer-I test score (without anaesthesia) • TBUT • Complete corneal clearing • Artificial tear use • Investigator global evaluation of efficacy Safety Outcomes • Grade 3/4 adverse events (AE) only • Overall incidence of AE • Withdrawal due to AE • Serious adverse events (SAE) • Individual AE: blepharitis, eye irritation, instillation site pain, eye pain, conjunctival hyperaemia, and nasopharyngitis
Study Design	Randomised controlled trials (RCTs)

The CS notes that during the screening of full publications, review discrepancies in the reporting of patient severity were noted. To ensure consistency across the studies, the Dry Eye Workshop (DEWS) 2007 dry eye severity grading scheme was used. Where studies pre-dated the publication of DEWS 2007 or alternative diagnostic measures were used, severity was determined based on Schirmer's test score, tear-film break-up time (TBUT) and/or Ocular Surface Disease Index (OSDI) (from the study's eligibility criteria or baseline characteristics). If disease severity was unclear, studies were appropriately excluded.

However, the CS notes that these criteria were not always strictly adhered to. Three studies were in fact included for other reasons where a severe DED population was indicated based on TBUT and baseline values or Schirmer's test score and CFS; one of these studies also stated "56 patients with severe keratoconjunctivitis sicca were enrolled".

Identified Studies

The company's search yielded 1726 citations, of which 31 studies were included in its systematic review. However, in the CS the company only presents evidence for two phase III trials (SANSIKA and SICCANOVE), both of which compared Ikervis to a vehicle and both of which were sponsored by the company. A third trial of Ikervis, a phase IIb trial (ORA) was excluded by the company. During the clarification process the company explained that ORA had been excluded because patients in that trial had mild to moderate DED and, therefore, the company did not consider the study to be pivotal or results supportive to the research question. The ERG agrees with this reasoning.

Studies Identified by the ERG's Search

The ERG's own searches identified two published systematic reviews of CsA for DED (of any severity). These included a total of 20 RCTs, three of which were included in the standalone systematic review. However, none of the RCTs identified from the ERG's searches included Ikervis as an intervention or comparator and so are not directly relevant to this appraisal.

In addition to the two completed systematic reviews, the ERG's searches also identified a protocol for a Cochrane Review which is currently in progress. During the clarification process the company confirmed that it had not contacted the authors of this review. Contacting the authors of ongoing reviews is often a good method for ensuring all relevant trials are identified. However, given the company is the sponsor of Ikervis, the ERG is confident that all relevant Ikervis trials have been identified in this instance.

Cost-effectiveness

ERG Comment on Company's Review of Cost-effectiveness Evidence

Objective of the Cost-effectiveness Review

Details of the search strategies employed by the company are included in the CS. Medline (via OVID SP), Medline R-In Process (via OVID SP), Econ-Lit (via OVID SP) and EMBASE (via OVID SP) searches were undertaken. Additionally, searches of the National Health Service Economic Evaluation Database (NHS EED) and the Cochrane Database of Abstracts and Reviews of Effects (DARE) were performed. The time horizon for the searches was database inception (Medline 1946; EMBASE 1974; EconLIT 1998; NHS EED 1960) to 15th July 2014.

Eligibility Criteria Used in Study Selection

The inclusion criteria used in the company's study selection are presented in the table below. The ERG is satisfied that these criteria are relevant to the decision problem.

Economic Evidence Search Inclusion Criteria Used by the Company

	Inclusion Criteria
Patients	People with severe dry eye disease (DED) whose disease has not adequately responded to tear substitutes
Subgroups	None
Interventions	Ikervis
Study type	Cost-effectiveness and cost-utility analyses
Country	UK, US and EU5
Year of Publication	2012 onwards

Included and Excluded Studies

No relevant studies were identified by the company.

ERG Critique of the Company's Literature Review

The ERG is satisfied with both the company's search strategy and their review inclusion criteria, and is confident that the company did not miss any relevant published papers. The ERG notes that since CsA has not yet received a full marketing authorisation from the European Medicines Agency (EMA) for the treatment of DED, the lack of economic evaluations of relevance to the decision problem is not unexpected.

Number of Source Documents

Clinical Effectiveness

Two randomised controlled trials (RCTs) were included.

Cost-effectiveness

- No relevant published studies were identified.
- The company submitted an economic model.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by Liverpool Reviews & Implementation Group (LRiG) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Data Abstraction Strategy

Data were appropriately extracted by a single reviewer and cross-checked by a second reviewer.

Quality Assessment

The completed tool used for quality assessment is presented in the company's submission (CS). Quality assessment included elements of the tool for assessing risk of bias recommended by the Cochrane Collaboration. The ERG agrees this is an appropriate tool for assessing the quality of randomised controlled trials (RCTs).

Evidence Synthesis

The trials included in the company's systematic review had heterogeneous populations. Hence, the majority of the evidence was, therefore, appropriately presented narratively. Data for Corneal Fluorescein Staining-Ocular Surface Disease Index (CFS-OSDI) response reported for patients with Sjögren's syndrome and for treatment-emergent adverse events (AEs) for all patients were, however, pooled. In both instances this appears to have been carried out to improve precision of estimates.

Description and Critique of the Statistical Approach

Pooled Data from SANSIKA and SICCANOVE

Meta-analyses were presented in the CS for CFS-OSDI response at month 6 using imputed data in the Sjögren's syndrome set in from the fool analysis set (FAS) and in severe FAS (CFS = 4 and OSDI ≥23); the ERG notes that the definition of severe dry eyes disease (DED) here differs slightly to that used for SICCANOVE alone (CFS ≥3 and OSDI ≥23 or CFS = 4). The ERG requested clarification on the methods used and whether the analysis was pre-specified. The company responded that the analysis was specified in 2012, a time when the results of the SICCANOVE trial were available but the SANSIKA trial was still blinded. The company stated that a fixed effects model had been used. The ERG also notes that descriptive post-hoc subgroup meta-analyses results for the change in CFS score in the FAS population according to age, gender, menopausal and Sjögren's status, age and duration of the disease are also reported in the draft European public assessment report (EPAR). Additional meta-analyses were also provided during the clarification process. Only the meta-analyses presented in the CS for the subgroup of patients with severe DED and Sjögren's syndrome (severe FAS) are considered relevant to the decision problem by the ERG.

The ERG notes that in the company's presentation of the results, the forest plot lacks important detail commonly reported with the presentation of meta-analyses such as the weight given to each study and a test for heterogeneity (such as I^2). As such, the ERG has some concerns that the data may have been simply pooled by adding the data together rather than using standard techniques for conducting meta-analyses. This would also mean that the randomisation in the individual studies is unlikely to be preserved.

AE data were also pooled to assess safety. During the clarification process, the company confirmed that no specific meta-analysis model was used for the analysis and descriptive statistics were provided. However, the ERG also notes the data presented include an estimate for relative risk between treatment arms, implying statistical analyses were conducted that were not simply descriptive.

Refer to Section 4 of the ERG report (see the "Availability of Companion Documents" field) for more information about clinical effectiveness analysis.

Cost-effectiveness

Model Structure

A schematic of the company's model is provided in the CS and reproduced in Figure 1 of the ERG report. It is a state transition (Markov) model with a cycle length of 3 months and is largely populated with data from the SANSIKA trial. All patients enter the model in the 'treatment induction' health state where they receive Ikervis plus artificial tears or artificial tears alone. They remain in this state for 6 months, after which they move to either the 'treatment responders' health state or the 'non-responders' health state. To be classified as a responder, an OSDI improvement from baseline of at least 30% as well as a CFS improvement from baseline of three or more is required. Patients in the 'treatment responders' health state remain in that state and continue on their assigned therapy until that therapy is no longer efficacious. When therapy is no longer efficacious patients move to the non-responders health state. Patients in the non-responders health state either stay in that state (receiving artificial tears alone) or temporal punctal plugs are trialled. Those patients who respond well to the temporal punctal plugs progress to having that treatment made permanent and progress to the 'Post plugs' state.

Refer to Sections 5 and 6 of the ERG report (see the "Availability of Companion Documents" field) for additional information about cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Care Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the Appraisal Consultation Document (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE Web site. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the Final Appraisal Determination (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions

Availability and Nature of Evidence

The Committee considered the cost-effectiveness evidence presented by the company for ciclosporin plus artificial tears compared with artificial tears alone. It noted that the company used the results from the vehicle group in SANSIKA as a proxy to model the results of artificial tears alone and that the company stated that the response or reduction in the use of artificial tears in the vehicle group was viewed as a regression to the mean.

The Committee noted that the company had provided the amendments it requested in the appraisal consultation document by presenting an updated economic model that compared ciclosporin plus corticosteroids (if needed) and artificial tears with vehicle plus corticosteroids (if needed) and artificial tears.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

The Committee noted that the company's updated model included corticosteroids as a cost parameter only and that results from the vehicle group in SANSIKA were still used as a proxy for the comparator group in the model. The Committee concluded that the company's original and updated model were only of limited relevance because they failed to show the cost-effectiveness of ciclosporin compared with established clinical practice in the National Health Service (NHS), that is corticosteroids (if needed) plus artificial tears.

The Committee restated its concerns about the company's post hoc analyses of SANSIKA and concluded it was more appropriate to use the original Corneal Fluorescein Staining-Ocular Surface Disease Index (CFS-OSDI) response data in the model.

The Committee concluded that it was unclear when treatment with ciclosporin would be stopped in clinical practice because corticosteroids' potential effect on stopping rates had not been included in the company's updated model.

The Committee recognised that the cost-effectiveness results varied substantially when applying treatment-specific utility values but was also aware that the analyses did not capture corticosteroids' potential to mitigate adverse effects. The Committee concluded that this added additional uncertainty to the results presented by the company.

Incorporation of Health-related Quality-of-Life Benefits and Utility Values. Have Any Potential Significant and Substantial Health-related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

The Committee noted that the company used pooled EuroQoL 5D questionnaire (EQ-5D) data from SANSIKA for both response and non-response.

The company highlighted that ciclosporin was particularly beneficial because it is administered as 1 eye drop per day compared with other treatments that need to be provided several times per day. The company stated that the benefits in terms of administration had not been appropriately captured in the quality-adjusted life year (QALY) calculation.

Are There Specific Groups of People for Whom the Technology Is Particularly Cost Effective?

The Committee noted that the company provided a subgroup analysis for people with Sjögren's syndrome in its updated model. However, this subgroup analysis incorporated the same assumptions as the analysis for all patients and the Committee concluded that these results also lacked relevance for its decision-making.

What Are the Key Drivers of Cost-effectiveness?

The Committee noted that 3 parameters had a substantial effect on the cost-effectiveness results (namely, using the original or post-hoc CFS-OSDI response definition, a 3- or 6-month stopping rule, and pooled or different utility values for treatment groups) and that changing them led to very variable results.

Most Likely Cost-effectiveness Estimate (Given as an Incremental Cost-effectiveness Ratio [ICER])

The Committee concluded that the company's original and updated model were only of limited relevance because they failed to show the cost

effectiveness of ciclosporin compared with established clinical practice in the NHS, that is corticosteroids (if needed) plus artificial tears.

The Committee agreed that it was relevant to consider ciclosporin (Ikervis) in comparison with other ciclosporin formulations available. The Committee considered that the different ciclosporin formulations would show similar efficacy and concluded that, based on the cost-minimisation analyses presented by the company and the ERG, the cost of ciclosporin (Ikervis) was reasonable compared with the other ciclosporin formulations.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination (FAD).

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Appraisal Committee considered clinical and cost-effectiveness evidence submitted by the manufacturer of ciclosporin and a review of this submission by the Evidence Review Group (ERG). The main clinical effectiveness evidence came from two randomised controlled trials (RCTs). For cost-effectiveness, the Appraisal Committee considered an economic model submitted by the manufacturer.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate use of ciclosporin for treating dry eye disease (DED) that has not improved despite treatment with artificial tears

Potential Harms

The most common adverse reactions with ciclosporin are eye pain, eye irritation, lacrimation, ocular hyperaemia, and eyelid erythema.

For full details of adverse reactions and contraindications, see the summary of product characteristics.

Refer to Appendix 2 of the Evidence Review Group (ERG) report (see the "Availability of Companion Documents" field) for additional data on adverse events reported in clinical trials.

Contraindications

Contraindications

For full details of contraindications, see the summary of product characteristics.

Qualifying Statements

Qualifying Statements

- This guidance represents the views of the National Institute for Health and Care Excellence (NICE) and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

- Section 7(6) of the National Institute for Health and Care Excellence (NICE) (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, National Health Services (NHS) England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.
- The Welsh Assembly Minister for Health and Social Services has issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 3 months of the guidance being published.
- When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has dry eye disease which has not improved despite treatment with artificial tears and the doctor responsible for their care thinks that ciclosporin is the right treatment, it should be available for use, in line with NICE's recommendations.
- NICE has developed tools to help organisations put this guidance into practice (listed below).
    - Costing template and resource impact report to estimate the national and local savings and costs associated with implementation.

Implementation Tools

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Ciclosporin for treating dry eye disease that has not improved despite treatment with artificial tears. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Dec 16. 45 p. (Technology appraisal guidance; no. 369).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015 Dec 16

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

Committee Members: Professor Andrew Stevens (*Chair of Appraisal Committee C*), Professor of Public Health, University of Birmingham; Professor Eugene Milne (*Vice Chair of Appraisal Committee C*), Director of Public Health, City of Newcastle upon Tyne; Professor Kathryn Abel, Institute of Brain and Behaviour Mental Health, University of Manchester; Dr David Black, Medical Director, NHS South Yorkshire and Bassetlaw; David Chandler, Lay member; Gail Coster, Advanced Practice Sonographer, Mid Yorkshire Hospitals NHS Trust; Professor Peter Crome, Honorary Professor, Dept of Primary Care and Population Health, University College London; Professor Rachel A Elliott, Lord Trent Professor of Medicines and Health, University of Nottingham; Dr Nigel Langford, Consultant in Clinical Pharmacology and Therapeutics and Acute Physician, Leicester Royal Infirmary; Dr Patrick McKiernan, Consultant Pediatrician, Birmingham Children's Hospital; Dr Suzanne Martin,

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Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in ePub and eBook formats from the NICE Web site .

Availability of Companion Documents

The following are available:

- Ciclosporin for treating dry eye disease that has not improved despite treatment with artificial tears. Resource impact report. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Dec. 8 p. (Technology appraisal guidance; no. 369). Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Ciclosporin for treating dry eye disease that has not improved despite treatment with artificial tears. Resource impact template. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Dec. (Technology appraisal guidance; no. 369). Available from the NICE Web site .
- Fleeman N, Bagust A, Beale S, Boland A, Dwan K, Kotas E, McEntee J, Ahmad S. Ciclosporin for treating dry eye disease: a single technology appraisal. Liverpool (UK): Liverpool Reviews & Implementation Group (LRiG), University of Liverpool; 2015 Mar. 91 p. Available from the NICE Web site .
- Ciclosporin for the treatment of severe keratitis in adult patients with dry eye disease that has not improved despite treatment with tear substitutes. Single technology appraisal. Manufacturer's submission. Santen GmbH; 2015 Feb. 256 p. Available from the NICE Web site .

Patient Resources

The following is available:

- Ciclosporin for treating dry eye disease that has not improved despite treatment with artificial tears. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Dec. 2 p. (Technology appraisal guidance; no. 369). Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in ePub and eBook formats from the NICE Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide

specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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